Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Koreth J, Matsuoka K-i, Kim HT, et al. Interleukin-2 and regulatory T cells in graft-versus-host disease. N Engl J Med 2011;365:2055-66.

Supplementary Appendix

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Supplementary Table Legend:

Supplementary Tables: Additional information on each study participant.

(A) Patient and disease characteristics, with IL-2 dose-levels. Sentinel sites of cGVHD are in **bold**. (B) IL-2 response with IL-2. Clinical responses during 8 week IL-2 and patients on extended-duration IL-2 are indicated, including adverse effects (with attribution; IL-2-related in **bold**), clinical response to 8 week and extended-duration IL-2, and description of relevant toxicities and response. Numerical cGVHD organ specific and global scores (NIH consensus criteria) are indicated for patients with clinical benefit. For global ratings and categorical scales, a 1 point change on a 3 or 7 point scale, or a 2 point or greater change on a 0 to10 point scale are considered clinically meaningful.

* sites not scored for response as topical therapy changes permitted during 8 week IL-2 therapy.

ADL: activities of daily living

AE: adverse effect

CAD: coronary artery disease

CNI: calcineurin inhibitor

DM: diabetes mellitus

DVT: deep vein thrombosis

ECP: extracorporeal photopheresis

GI: gastrointestinal

J/F/M: joint/fascia/muscle

LV: left ventricle

MI: myocardial infarction

MMF: mycophenolate mofetil

MRSA: methicillin resistant Staphylococcus aureus

NE: non evaluable

NQWMI: non Q-wave mycardial infarction

PR: partial response per NIH consensus criteria

SD: stable disease per NIH consensus criteria

TMA: thrombotic microangiopathy

Supplementary Table-A

ID	Age	Days post-HSCT	Days post-cGVHD	cGVHD sites	Concurrent cGVHD therapy	Discontinued prior therapies	IL-2 dose-level
1	34	1483	1267	**Skin,** Eyes*, Liver, Mouth*	CNI, Sirolimus, Steroids	Rituximab	A
2	40	579	424	**Skin**, Eyes*, J/F/M, Lung, Mouth*	CNI, MMF, Steroids		A
3	57	420	117	**Liver**	MMF, Sirolimus, Steroids		A
4	53	1734	1275	**Skin,** Mouth*	CNI, Sirolimus, Steroids	MMF, Thalidomide	A
5	44	1021	784	**Skin,** Peripheral nerves	MMF, Sirolimus, Steroids		A
6	61	1425	1186	**Skin**, Eyes*, Liver, Mouth*	CNI, Sirolimus, Steroids	ECP, MMF, Rituximab	A
7	41	823	161	**Skin**	CNI, Steroids	Rituximab, Sirolimus	A
8	60	2766	2624	**Skin**, J/M/F	MMF, Sirolimus, Steroids	Alemtuzumab, CNI, Denileukin diftitox, ECP, Rituximab	B
9	63	2734	2233	**Skin**, Mouth*	MMF, Steroids	ECP, Rituximab, Sirolimus	B
10	48	1575	1127	**Skin**, J/F/M	Steroids	ECP, Rituximab	B
11	46	776	450	**Skin, J/F/M,** Eyes* Lung, Mouth*	Steroids		B
12	55	969	821	**Skin, J/F/M**	CNI, Sirolimus, Steroids	Alemtuzumab, MMF, Rituximab	C
13	27	525	192	**Liver**, Eyes*, Lung, Mouth*	MMF, Sirolimus, Steroids		C
14	65	728	502	**Skin, J/F/M**	MMF, Sirolimus, Steroids	CNI	C
15	38	1996	1358	**Skin,** Eyes*, Liver, Lung, Mouth*	MMF, Steroids	ECP, Rituximab	B
16	38	734	490	**Skin,** Lung	CNI, MMF, Sirolimus	ECP, Rituximab, Steroids	B
17	64	2539	2400	**Skin, J/F/M,** Eyes*	CNI, MMF, Steroids	ECP, Imatinib, Rituximab	B
18	54	841	452	**Skin, J/F/M,** Eyes*	CNI, Sirolimus, Steroids	ECP, MMF, Rituximab	B
19	51	1135	763	**Lung**	MMF, Steroids	CNI, Sirolimus	B
20	55	1293	1050	**Skin, J/F/M ,** Eyes*, Mouth*	Steroids	Alemtuzumab, ECP, Imatinib	B
21	28	1094	556	**Skin, J/F/M**, Eyes*, Mouth*	Steroids	CNI, ECP, Imatinib, Rituximab	B
22	54	1559	1403	**Skin, J/F/M ,** Eyes*, Mouth*	CNI, Steroids	MMF, Rituximab	B
23	52	1567	1274	**Skin, J/F/M,** Eyes*, Mouth*	CNI, MMF, Steroids	Sirolimus	B
24	68	2351	1569	**Skin, J/F/M**, Eyes*	Imatinib, MMF, Steroids	ECP	B
25	52	1110	609	**Skin, J/F/M,** Eyes*	CNI, MMF, Steroids	Bortezomib, Rituximab	B
26	34	903	756	**Skin J/F/M,** Eyes*	Imatinib, MMF, Steroids	Rituximab	B
27	22	747	487	**Skin, J/F/M,** Eyes*	CNI, Sirolimus, Steroids	ECP, Imatinib, MMF, Rituximab	B
28	37	1420	876	**Skin,** Mouth*	MMF, Steroids	Rituximab	B
29	26	1699	1443	**Skin, J/F/M,** Eyes*, Mouth*	CNI, MMF, Steroids	Dasatinib, ECP, Etanercept, Imatinib, Rituximab	B

Supplementary Table-B

ID	8 Week Response per NIH criteria	AEs: CTC grade ≥3; or IL-2-associated (grade: attribution)	Extended IL-2 (months): NIH organ score Prednisone taper	Response and Toxicity Description
1	NE	Hemophilus influenzae type B bacteremia (Gr 3: unrelated); **TMA (Gr. 4-DLT: prob. related)**	N/A	1. Softening of sclerodermatous skin at 4 week IL-2. 2. AEs: - Hemophilus B bacteremia after 4-week IL-2. IL-2 withheld. - TMA at 12 days off IL-2.
2	Yes: PR Skin 3→2 J/F/M 2→1 Global: 9→7		Yes-ongoing (36): Skin-1; J/F/M-0 Prednisone: 80mg→ off	1. 8-week IL-2: appreciable softening of hidebound skin; improved joint mobility. 2. Extended IL-2: continued improvement.
3	Yes: PR Liver 3→2 Global: 5→3	MRSA pneumonia (Gr. 4: unrelated)	No	1. 8-week IL-2: 50% improvement in liver cGVHD (total bilirubin 12.3→ 6). 2. Could not receive extended IL-2 due to MRSA pneumonia at 8 weeks of IL-2 (similar infection prior to IL-2 too). 3. Died of liver GVHD (peak bilirubin 84.8) ~3 months off-IL-2.
4	No: SD		No	
5	Yes: PR Skin 3→2 Nerves-CR Global: 7→4		Yes-ongoing (30): skin-1 Prednisone: 30 mg→ off	1. 8-week IL-2: resolution of neuropathic pain; gait improvement; softening of sclerodermatous skin. 2. Extended IL-2: continued improvement.
6	No: SD		No	
7	No: SD		No	
8	No: SD		No	
9	NE		N/A	1. IL-2 discontinued at 4 days per patient preference.
10	Yes: PR Skin 3→2 J/F/M 3→2 Global 8→5		Yes-complete (14): skin-0; J/F/M-0 Prednisone: 20 mg→ off, and off IL-2	1. 8-week IL-2: considerable softening of hidebound skin, improved joint mobility. 2. Extended IL-2: CR at 14 months.
11	Yes: PR Skin 3→2 J/F/M 2→1 Global 7→5		Yes-ongoing (22): skin-1; J/F/M-0 Prednisone: 20 mg→15 mg	1. 8-week IL-2: considerable softening of hidebound skin; improved joint mobility. 2. Extended IL-2: continued improvement.
12	No: SD (minor response) Skin 2→2	**Injection-site induration (Gr. 3: related)**	Yes-stopped (1.5): skin-2; J/F/M-3	1. 8-week IL-2: patient subjective improvement in joint mobility and chose extended IL-2. 2. Extended IL-2: discontinued at 6 weeks given no further improvement

	J/F/M 3→3 Global 8→7			
13	No: SD		No	
14	Yes: PR Skin 3→2 J/F/M 2→1 Global 6→4	**Injection-site induration (Gr. 3: related)**	Yes-ongoing (15): skin-1; J/F/M-1 Prednisone: 10 mg→7.5 mg	1. 8-week IL-2: considerable softening of hidebound skin; improved joint mobility; decreased edema; much improved pain. 2. Extended IL-2: continued improvement
15	NE	DOE/SOB (Gr. 4: unrelated)	N/A	1. IL-2 withheld at 4 weeks for acute onset dyspnea/pneumonitis (multifactorial).
16	NE	**Renal (Gr. 2: possibly related)**	N/A	1. Baseline renal dysfunction (Cr 1.9 mg/dl), off-study at 3-weeks of IL-2 due to increased renal dysfunction (Cr 2.6 mg/dl) possibly related to IL-2.
17	No: SD (minor response) Skin 2→2 J/F/M 2→2 Global 6→5		Yes-stopped (4): skin-2; J/F/M-2	1. 8-week IL-2: minimal softening of sclerodermatous skin; patient chose extended IL-2. 2. Extended IL-2: discontinued at 4 months given no further improvement
18	NE	**TMA (Gr. 4-DLT: probably related)**		1. Eligibility subsequently amended to exclude baseline renal dysfunction, or concomitant sirolimus plus CNI.
19	No: SD (minor response) Lung 1→1 Global 3→2		Yes-ongoing (12); Lung-1 Prednisone: 10 mg →off, and off MMF	1. 8-week IL-2: patient subjective breathing improvement, walking ~3 miles/day; stable PFTs (PR per NIH criteria, but scored as SD). 2. Extended IL-2: stable PFTs. Feels normal, walks up to 5 miles/day.
20	NE	**Thrombocytopenia (Gr. 2: possibly related)**	N/A	1. Softening of sclerodermatous skin at 4-week IL-2, but off-study due to AE concern. 2. IL-2 discontinued at 4 weeks due to thrombocytopenia/schistocytosis without renal or neurological impairment, concerning for possible incipient TMA.
21	Yes: PR Skin 3→2 J/F/M 3→2 Global 9→7	MRSA abscess (Gr. 3: unrelated); **Constitutional: fevers, fatigue (Gr. 2: probably related)**	No	1. 8-week IL-2: considerable improvement of anasarca; ~90% healing of extensive ulcerated leg lesions; and sclerodermatous skin softening. 2. AE: - MRSA buttock furuncle prior to IL-2 initiation (patient omitted to mention). IL-2 withheld starting day 2 for incision/drainage and 3.5 weeks of antibiotic therapy. 3. Could not proceed on extended IL-2 due to inability to return for follow-up and constitutional side-effects.
22	Yes: PR Skin 3→2 J/F/M 2→1	Lower GI Bleed (Gr. 3: unrelated);	No	1. 8-week IL-2: considerable softening of hidebound sclerodermatous skin, improved joint mobility. 2. AEs:

	Global: 7→6	DVT/LV thrombus (Gr. 3: unrelated)		- Lower GI bleed at 7 weeks of IL-2 likely related to diverticular disease. IL-2 withheld. - Leg DVT at 21 days off IL-2, likely related to GI bleed-associated restricted mobility. Incidental focal left ventricular hypokinesis-associated thrombus during DVT work up, likely due to non-acute MI of indeterminate age. - Death from acute MI at 70 days off IL-2.
23	Yes: PR Skin 2→1 J/F/M 2→1 Global 6→4	Acute MI (Gr. 4: unrelated)	Yes-ongoing (4) : skin-1; J/F/M-1 Prednisone: 20 mg→15 mg	1. 8-week IL-2: considerable softening of sclerodermatous skin, improved mobility. 2. AEs: - Acute NQWMI requiring coronary stents at 2 weeks of IL-2. Prior CAD, DM, hyperlipidemia, CAD family history. IL-2 withheld for 1 week. LV function preserved. - NQWMI with in-stent thrombosis at 6 weeks of extended IL-2 therapy. Re-stented. LV function preserved. IL-2 withheld for 4 weeks, then restarted. 3. Extended IL-2: continued improvement- further softening and reduced extent of hidebound skin.
24	Yes: PR Skin 2→1 J/F/M 2→1 Global 5→3		Yes-ongoing (4) : skin-1; J/F/M-1 Prednisone 25 mg→15 mg	1. 8-week IL-2: considerable softening of sclerodermatous skin, improved joint mobility. 2. Extended IL-2: continued improvement- further softening and reduced extent of hidebound skin.
25	No: SD		No	
26	No: SD	**Injection-site induration (Gr. 3: related)**	No	
27	Yes: PR Skin 3→2 J/F/M 3→1 Global 9→7		Yes-ongoing (3): skin-2; J/F/M-1 Prednisone: 20 mg→5 mg	1. 8-week IL-2: considerable softening of sclerodermatous hidebound skin, shrinkage of ulcers, and improved joint mobility. Improved ambulation and ADL capacity. 2. Extended IL-2: continued improvement- further skin softening, re-growth of adnexae (hair), healing of extensive deep ulcers, improving ambulation.
28	No : SD		No	
29	Yes: PR Skin 3→2 J/F/M 3→2 Global 10→8		Yes-ongoing (2) Prednisone: 15 mg→10 mg	1. 8-week IL-2: considerable softening of extensively hidebound skin, decreased erythema and discharge. Improved joint mobility, ambulation and ADL capacity. 2. Extended IL-2: continued improvement- further skin softening, decreasing discharge, improved mobility and ambulation. cGVHD assessment not yet due.

Additional Correlative Analyses:

Response (PR) was associated with baseline Treg:Tcon ratio, with a median of 0.09 (IQR: 0.07-0.12) in responders versus 0.05 (IQR, 0.04-0.1) in non-responders (p=0.03). When stratified by baseline median Treg:Tcon ratio (0.07), patients with ratios above the median had a 75% response rate compared with 20% in those with below median ratios (p=0.03). The sensitivity, specificity, and positive predictive value were 82%, 73% and 75%, respectively, though the numbers are small.

While Treg increased in both responders and non-responders, after 8 weeks of IL-2 therapy the median Treg count was 175 for responders and 75 for non-responders (p=0.11), with a median Treg rise above baseline of 174 for responders and 45 for non-responders (p=0.08). After 4 weeks off IL-2 therapy, the median Treg count was 42 for responders and 15 for non-responders (p=0.08). In this small series, these findings are not statistically significant.

Treg Changes with Alternative Therapy:

To address the possibility that in-vivo Treg expansion might occur non-specifically in patients as cGVHD improves, we examined changes in CD4+CD25+ Treg in a series of patients previously enrolled on a clinical protocol to assess the safety and efficacy of rituximab for treatment of active glucocorticoid-refractory cGVHD (Cutler et al. Blood 2006; 108(2): 756–762). In this clinical trial, changes in CD4+CD25+ Treg were monitored prospectively, along with changes in CD3+ T cells, CD8+ T cells and CD19+ B cells.

Analysis of blood samples in 16 responding patients showed no increase in Treg. Specifically, median Treg counts (cells/µl) at baseline and 8, 16, 26 and 52 weeks on study were as follows: 30 (IQR, 6-83), 16 (IQR, 7-91), 16 (IQR, 7-23), 11 (IQR, 7-45) and 31 (IQR, 14-43) respectively (p=ns). Similar results were observed in non-responders on this study.

Our results indicate that there was no statistically significant change in CD4+CD25+ Treg in clinical responders or non-responders on this trial. These results suggest that Treg expansion does not occur in patients with cGVHD who respond to therapies not specifically designed to affect Treg *in-vivo*.

IL-2 for cGVHD

Provider Survey

Enrollment

Instructions:
Please score a symptom only if you know or suspect it be *related to chronic GVHD*. Subjective symptoms are acceptable. For example, joint tightness can be scored based on subjective findings despite the absence of objective limitations.

Please score symptoms present in the *last week*. Even if they may have resolved with treatment in the past week, if they were present recently and may possibly return, please score them.

Date of Visit: _____

Patient: _____

MRN: _____

cGVHD Dx Date: _____

Your Name: _____

Check ONE area of the body as the sentinel lesion		Erythematous rash of any sort	Moveable sclerosis	Non-moveable subcutaneous sclerosis or fasciitis
1. Head/neck/scalp	❑	%	%	%
2. Anterior torso	❑	%	%	%
3. Posterior torso	❑	%	%	%
4. L. upper extremity	❑	%	%	%
5. R. upper extremity	❑	%	%	%
6. L. lower extremity, (incl. L buttock)	❑	%	%	%
7. R. lower extremity, (incl. R buttock)	❑	%	%	%
8. Genitalia ❑ not examined	❑	%	%	%

	0	1	2	3	4
Skin sclerotic changes	❑ Normal	❑ Thickened with pockets of normal skin	❑ Thickened over majority of skin	❑ Thickened, unable to move	❑ Hidebound, unable to pinch

	0	**1**	**2**	**3**
Skin Score	❑ No Symptoms	❑ <18% BSA with disease signs but **NO** sclerotic features	❑ 19-50% BSA **OR** involvement with superficial sclerotic features "not hidebound" (able to pinch)	❑ >50% BSA **OR** deep sclerotic features "hidebound" (unable to pinch) **OR** impaired mobility, ulceration or severe pruritus
Fascia	❑ Normal	❑ Tight with normal areas	❑ Tight	❑ Tight, unable to move

Clinical Skin Features	
❑ Ulcer Location: _____	Largest dimension: _____ cm
❑ Maculopapular rash	❑ Keratosis pilaris
❑ Lichen planus-like lesions	❑ Papulosquamous lesions or icthyosis
❑ Poikiloderma	❑ Hair involvement
❑ Pruritus	❑ Nail involvement
❑ Other, specify:	❑ Other, specify:

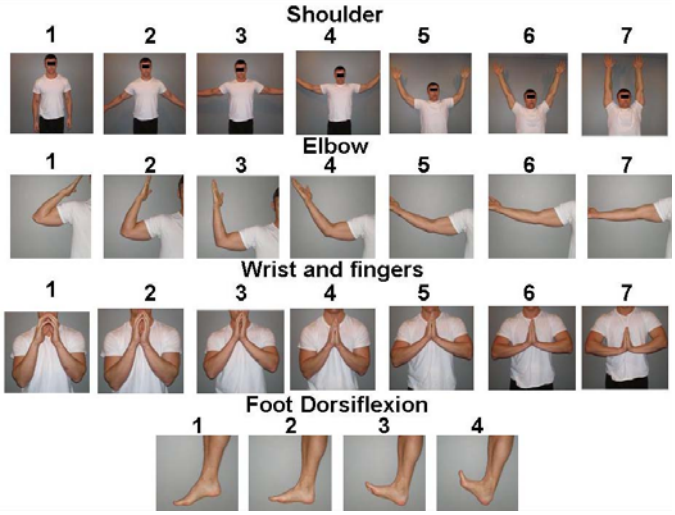
Region	Grade	% Area of Grade	Fraction of Grade 3 or 4 Areas with Erythema (indicate up to what fraction is involved)	Region	Grade	% Area of Grade	Fraction of Grade 3 or 4 Areas with Erythema (indicate up to what fraction is involved)
1. Head, Neck and Scalp ❑	0	%		6. Right Hand ❑	0	%	
	1	%			1	%	
	2	%			2	%	
	3	%	❑0 ❑¼ ❑½ ❑¾ ❑1		3	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	4	%	❑0 ❑¼ ❑½ ❑¾ ❑1		4	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	Total =	**100 %**			**Total =**	**100 %**	
2. Chest ❑	0	%		7. Left Arm ❑	0	%	
	1	%			1	%	
	2	%			2	%	
	3	%	❑0 ❑¼ ❑½ ❑¾ ❑1		3	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	4	%	❑0 ❑¼ ❑½ ❑¾ ❑1		4	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	Total =	**100 %**			**Total =**	**100 %**	
3. Abdomen and Genitals ❑	0	%		8. Left Hand ❑	0	%	
	1	%			1	%	
	2	%			2	%	
	3	%	❑0 ❑¼ ❑½ ❑¾ ❑1		3	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	4	%	❑0 ❑¼ ❑½ ❑¾ ❑1		4	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	Total =	**100 %**			**Total =**	**100 %**	
4. Back and Buttocks ❑	0	%		9. Right Leg and Foot ❑	0	%	
	1	%			1	%	
	2	%			2	%	
	3	%	❑0 ❑¼ ❑½ ❑¾ ❑1		3	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	4	%	❑0 ❑¼ ❑½ ❑¾ ❑1		4	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	Total =	**100 %**			**Total =**	**100 %**	
5. Right Arm ❑	0			10. Left Leg and Foot ❑	0		
	1				1		
	2				2		
	3		❑0 ❑¼ ❑½ ❑¾ ❑1		3	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	4	%	❑0 ❑¼ ❑½ ❑¾ ❑1		4	%	❑0 ❑¼ ❑½ ❑¾ ❑1
	Total =	**100 %**			**Total =**	**100 %**	

Check ONE area of the body as the sentinel lesion.

0 = normal skin
1 = discolored [hypopigmentation, hyperpigmentation, alopecia, erythema, maculopapular rash]
2 = lichenoid plaque, or skin thickened (able to move)
3 = skin thickened with limited motion but able to pinch [scleroderma or fasciae involvement]
4 = hidebound skin, unable to move, unable to pinch

ROM & MOUTH

Please circle this person's current ROM for each joint from 1=poor mobility to 7=full mobility below:



		0	1	2	3
Mouth Score		❑ No symptoms	❑ Mild symptoms with disease signs but not limiting oral intake significantly	❑ Moderate symptoms with signs with **partial** limitation of oral intake	❑ Severe symptoms with disease signs on examination with **major** limitation of oral intake
Mouth	**Erythema**	❑ None	❑ Mild erythema OR Moderate erythema (<25%)	❑ Moderate (≥25%) OR Severe erythema (<25%)	❑ Severe erythema (≥25%)
	Lichenoid	❑ None	❑ Hyperkeratotic changes (<25%)	❑ Hyperkeratotic changes (25-50%)	❑ Hyperkeratotic changes (>50%)
	Ulcers	❑ None	❑ None	❑ Ulcers involving (≤20%)	❑ Severe ulcerations (>20%)
	Mucoceles (of lower labia and soft palate only)	❑ None	❑ 1-5 mucoceles	❑ 6-10 scattered mucoceles	❑ Over 10 mucoceles
Mouth Pain		❑ No symptoms	❑ Food sensitivity	❑ Pain requiring narcotics	❑ Unable to eat

GASTROINTESTINAL

GI Tract Score		0	1	2	3
		❑ No symptoms	❑ Symptoms such as dysphagia, anorexia, nausea, vomiting, abdominal pain or diarrhea without significant weight loss (<5%)	❑ Symptoms associated with mild to moderate weight loss (5-15%)	❑ Symptoms associated with significant weight loss >15%, requires nutritional supplement for most calorie needs **OR** esophageal dilation
Gastro-intestinal	**Esophagus** • **Dysphagia OR** • **Odynophagia**	❑ No esophageal symptoms	❑ Occasional dysphagia or odynophagia with solid food or pills *during the past week*	❑ Intermittent dysphagia or odynophagia with solid food or pills (but not for liquids or soft foods) *during the past week*	❑ Dysphagia or odynophagia for almost all oral intake, *on almost every day of the past week*
	Upper GI • **Early satiety OR** • **Anorexia OR** • **Nausea & vomiting**	❑ No symptoms	❑ Mild, occasional symptoms with little reduction in oral intake *during the past week*	❑ Moderate, intermittent symptoms throughout the day, with some reduction in oral intake, *during the past week*	❑ More severe or persistent symptoms throughout the day, with marked reduction in oral intake, *on almost every day of the past week*
	Lower GI • **Diarrhea**	❑ No loose or liquid stools *during the past week*	❑ Occasional loose or liquid stools, on some days *during the past week*	❑ Intermittent loose or liquid stools through-out the day, *on almost every day of the past week* **without requiring** intervention to prevent or correct volume depletion	❑ Voluminous diarrhea *on almost every day of the past week* **requiring** intervention to prevent or correct volume depletion

OTHER ORGANS

	0	1	2	3
Eye Score	❑ No symptoms	❑ Mild dry eye symptoms not affecting ADL (requiring eye drops <3x per day) **OR** asymptomatic signs of kerato-conjunctivitis sicca	❑ Moderate dry eye symptoms partially affecting ADL (requiring eye drops >3x per day or punctual plugs) **WITHOUT** vision impairment	❑ Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain) **OR** unable to work because of ocular symptoms **OR** loss of vision caused by kerato-conjunctivitis sicca
Joints and Fascia Score	❑ No symptoms	❑ Mild tightness of arms or legs, normal or mild decreased range of motion (ROM) **AND** not affecting ADL	❑ Tightness of arms or legs **OR** joint contractures, erythema thought due to fasciitis, moderate decrease ROM **AND** mild to moderate limitation of ADL	❑ Contracture WITH significant decrease of ROM **AND** significant limitation of ADL (unable to tie shoes, button shirts, dress self etc.)
Genital Tract Score **❑ No GYN Exam** **NB: score still required**	❑ No symptoms	❑ Symptomatic with mild distinct signs on exam AND no effect on coitus and minimal discomfort with GYN exam	❑ Symptomatic with distinct signs on exam AND with mild dyspareunia or discomfort with GYN exam	❑ Symptomatic WITH advanced signs (stricture, labia agglutination or severe ulceration) AND severe pain with coitus or inability to insert vaginal spectrum
Lung Score	❑ No symptoms	❑ Mild symptoms (shortness of breath after climbing one flight of steps)	❑ Moderate symptoms (shortness of breath after walking on flat ground)	❑ Severe symptoms (shortness of breath at rest; requiring O_2)
Other Organ Score ***Specify:*** _____	❑ No effect on ADL	❑ Mild effect on ADL	❑ Moderate effect on ADL	❑ Severe effect on ADL
Other Organ Score ***Specify:*** _____	❑ No effect on ADL	❑ Mild effect on ADL	❑ Moderate effect on ADL	❑ Severe effect on ADL

Please rate the severity of this person's chronic GVHD	
on this scale →	❑ None (1) ❑ Mild (2) ❑ Moderate (3) ❑ Severe (4)
and on this scale → *(circle one)*	cGVHD symptoms are not at all severe … cGVHD symptoms are most severe possible 0 1 2 3 4 5 6 7 8 9 10

Reasons for changing therapeutic regimen (check all that apply)
❑ Not applicable, no changes made
❑ Adjust levels of medications
❑ Enroll on clinical trial
❑ Worsening of symptoms
❑ No improvement in symptoms
❑ Toxicity
❑ New symptoms
❑ Improvement in symptoms
❑ Disease relapse
❑ Stable

Sentinel Organ Response in which organ system will guide your treatment decisions (If more than one, please rank)
❑ Skin
❑ Joints
❑ Fascia
❑ Lung
❑ Urogenital
❑ Liver
❑ Mouth
❑ Esophagus
❑ Lower GI
❑ Other specify:

Does this person *currently* have:	❑ Late acute GVHD (1) ❑ Overlap acute and chronic GVHD (2) ❑ Classic chronic GVHD (3) ❑ No GVHD (0)

	0	**1**	**2**	**3**	**4**
Infection	❑ None	❑ Mild, topical or no therapy required	❑ Moderate, localized, requiring oral treatment For 2-4:	❑ Severe, systemic infection requiring IV anti-infective, mold-active oral antifungal or hospitalization	❑ Life-threatening infection
		❑ Pending lab report (1)	❑ Unidentified organism (2) ❑ Identified organism, specify (3):		

Peripheral Edema?	❑ None (0)	❑ Tr (9)	❑ 1+	❑ 2+	❑ 3+	❑ 4+

Other indicators, clinical manifestations or severe complications related to chronic GVHD					
	Never	**Past, not now**	**Mild**	**Moderate**	**Severe**
1. Pleural Effusion(s)	❑	❑	❑	❑	❑
2. Bronchiolitis obliterans	❑	❑	❑	❑	❑
3. Bronchiolitis obliterans organizing pneumonia	❑	❑	❑	❑	❑
4. Nephrotic syndrome	❑	❑	❑	❑	❑
5. Malabsorption	❑	❑	❑	❑	❑
6. Esophageal stricture or web	❑	❑	❑	❑	❑
7. Ascites (serositis)	❑	❑	❑	❑	❑
8. Myasthenia Gravis	❑	❑	❑	❑	❑
9. Peripheral Neuropathy	❑	❑	❑	❑	❑
10. Polymyositis	❑	❑	❑	❑	❑
11. Pericardial Effusion	❑	❑	❑	❑	❑
12. Cardiomyopathy	❑	❑	❑	❑	❑
13. Cardiac conduction defects	❑	❑	❑	❑	❑
14. Coronary artery involvement	❑	❑	❑	❑	❑
15. Other, please specify: _____	❑	❑	❑	❑	❑
16. Other, please specify: _____	❑	❑	❑	❑	❑
17. Other, please specify: _____	❑	❑	❑	❑	❑

For office use only:

Study ID	*Initials (First, Last)*	*Date completed:*	*Date received:*
Person completing form:		*Their degree:*	
Timepoint:		*Date entered:*	

v3.1